

WEST Search History

DATE: Monday, August 06, 2007

<u>Hide?</u>	<u>Set Name</u>	<u>Query</u>	<u>Hit Count</u>
<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=OR</i>			
<input type="checkbox"/>	L13	L12 not l4 not l2	55
<input type="checkbox"/>	L12	L8 same (anthrax or anthrac\$ or bacill\$).ti,ab,clm.	57
<input type="checkbox"/>	L11	L10 and (vegetative or cytoplasmic or cytoplasma or intracellular or signal or rrna or r-ma or l1)	445
<input type="checkbox"/>	L10	L8 same (anthrax or anthrac\$ or bacill\$)	622
<input type="checkbox"/>	L9	L8 and (anthrax or anthrac\$ or bacill\$)	1593
<input type="checkbox"/>	L8	L5 same (heterologous or heter-ologous or foreign or recombinantly or recombinant or engineering or delivery or fusion or chimeric or chimera or (expression near system))	2736
<input type="checkbox"/>	L7	L6 and (anthrax or anthrac\$ or bacill\$)	10325
<input type="checkbox"/>	L6	L5 and (heterologous or heter-ologous or foreign or recombinantly or recombinant or engineering or delivery or fusion or chimeric or chimera or (expression near system))	18806
<input type="checkbox"/>	L5	(\$spore or sporu\$ or spore\$)ti,ab,clm.	46588
<i>DB=EPAB,JPAB,DWPI; PLUR=YES; OP=OR</i>			
<input type="checkbox"/>	L4	L3 and (bacillus or spore or sporulation or vegetative or l1)	8
<input type="checkbox"/>	L3	cutting.in.	128
<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=OR</i>			
<input type="checkbox"/>	L2	L1 and (\$spore or spor\$ or \$spore\$)	7
<input type="checkbox"/>	L1	rrno or rrn-o or (rrn near o) or rrn0 or rrn-0 or (rrn near 0)	385

END OF SEARCH HISTORY

- 1. WO2006087576A1. 20 Feb 06. 24 Aug 06. LISTERIOLYSIN-CONTAINING BACILLUS SPORES AS ANTIGEN DELIVERY AGENTS. CUTTING, SIMON.
- 2. WO2005068493A1. 17 Jan 05. 28 Jul 05. ANTHRAX VACCINE IN THE FORM OF A SPORE. CUTTING, SIMON MICHAEL. C07K014/32; A61K039/07.
- 3. WO003074682A1. 07 Mar 03. 12 Sep 03. BACTERIAL SPORES. CUTTING, SIMON MICHAEL. C12N003/00; C12N015/03 C07K014/195 A61K035/74.
- 4. WO003074681A1. 07 Mar 03. 12 Sep 03. RECOMBINANT SPORES. CUTTING, SIMON MICHAEL. C12N003/00; C12N015/00 A61K039/00.
- 5. WO2006087576A. New non-pathogenic Bacillus spores comprising a polynucleotide sequence encoding a hemolysin, e.g. listeriolysin O, useful for treating, preventing, or ameliorating infection, autoimmune condition, allergy, or cancer. CUTTING, S. A61K039/39 C12N015/87.
- 6. WO2005068493A. New non-pathogenic spore comprising an antigenic fragment of anthrax protective antigen, useful as an anthrax vaccine or for manufacturing an anthrax vaccine. CUTTING, S M. A61K039/07 C07K014/32.
- 7. WO2003074682A. New genetically modified spores comprising at least one genetic construct encoding an antigen and a spore coat protein as a chimeric gene, useful in the treatment of inflammation, pain, a hormonal imbalance and/or an intestinal disorder. CUTTING, S M. A61K035/74 A61K039/00 A61K039/02 A61K039/08 A61K039/108 A61K048/00 A61P031/04 C07K014/195 C12N001/21 C12N003/00 C12N015/03 C12N015/09 C12N015/74.
- 8. WO2003074681A. New spore useful for treating pain and inflammation, is genetically modified with genetic code comprising at least one genetic construct encoding a therapeutically active compound and targeting sequence or vegetative cell protein. CUTTING, S M. A61K035/74 A61K038/00 A61K038/22 A61K038/43 A61K039/00 A61K039/02 A61K039/08 A61K048/00 A61P001/00 A61P005/00 A61P025/04 A61P029/00 A61P037/04 C12N001/21 C12N003/00 C12N015/00 C12N015/09.

[First Hit](#) [Fwd Refs](#)[Previous Doc](#) [Next Doc](#) [Go to Doc#](#) [Generate Collection](#) [Print](#)

L1: Entry 30 of 34

File: USPT

Nov 5, 1996

DOCUMENT-IDENTIFIER: US 5571698 A

** See image for Certificate of Correction **

TITLE: Directed evolution of novel binding proteins

Detailed Description Text (431):

It is believed that the conditions for an outer surface transport signal in a bacterial cell or spore are not particularly stringent, i.e., a random polypeptide of appropriate length (preferably 30-100 amino acids) has a reasonable chance of providing such a signal. Thus, by constructing a chimeric gene comprising a segment encoding the IPBD linked to a segment of random or pseudorandom DNA (the potential OSTs), and placing this gene under control of a suitable promoter, there is a possibility that the chimeric protein so encoded will function as an OSP-IPBD.

Detailed Description Text (434):

When the genetic package is a spore, we can use the approach described above for attaching a IPBD to an *E. coli* cell, except that: a) a sporulation promoter is used, and b) no periplasmic signal sequence should be present.

[Previous Doc](#) [Next Doc](#) [Go to Doc#](#)

Hit List

Parasporal

[First Hit](#) [Clear](#) [Generate Collection](#) [Print](#) [Fwd Refs](#) [Bkwd Refs](#)
[Generate OAICS](#)

Search Results - Record(s) 1 through 3 of 3 returned.

1. Document ID: US 20050089959 A1

L3: Entry 1 of 3

File: PGPB

Apr 28, 2005

DOCUMENT-IDENTIFIER: US 20050089959 A1

TITLE: Novel *Bacillus thuringiensis* strain, crystal gene and crystal protein and uses thereof

Brief Description of Drawings Paragraph:

[0052] FIG. 1 illustrates in panel A) a phase-contrast micrograph of a lysed culture of *Bacillus thuringiensis* strain M15; in panel B, a transmission electron micrograph of *Bacillus thuringiensis* strain M15 containing a spore and a tightly bound parasporal inclusion;

Brief Description of Drawings Paragraph:

[0058] FIG. 7 shows a transmission electron micrograph of a *B. thuringiensis* Cry.sup.- B transformant expressing the cry31Aa2 gene. S: spore; P: parasporal inclusion; Magnification: 20,000.times.;

Detail Description Paragraph:

[0063] A *Bacillus thuringiensis* strain was isolated from dead two-spotted spider mites (*Tetranychus urticae* Koch; Arthropoda: Arachnida: Tetranychidae) and named M15. The mites, parasitic on apple leaves, were collected in an apple orchard located in Freightsburgh, Quebec, Canada. They were homogenized in 3 ml of phosphate-buffered saline (PBS) (NaCl 8 g, KCl 0.2 g, Na₂HPO₄ 1.44 g, KH₂PO₄ 0.24 g I-1). The homogenized solution was incubated for 16 hr at room temp and heated at 78.degree. C. for 15 min. Afterwards, the homogenate was plated on 2YT agar medium (Bacto Tryptone 16 g, Bacto Yeast Extract 10 g, NaCl 5 g, Agar 18 g I-1), and incubated for 24 hr at 30.degree. C. All colonies with a morphology similar to *B. thuringiensis* were streaked on T3 agar medium (Bacto Tryptone 3 g, Bacto Tryptose 2 g, Bacto Yeast Extract 1.5 g, MnCl₂ 0.005 g, 0.05M Sodium phosphate, pH6.7, Agar 18 g I-1) and incubated at 30.degree. C. for 48 hr. The cultures were examined by phase-contrast microscopy (Carl Zeiss Canada Ltd., Toronto, Ontario, Canada) for the presence of spores and crystals. *B. thuringiensis* M15 was deposited on 29 January 2001 in the International Depository Authority of Health Canada in Winnipeg under the Budapest Treaty (Bureau of Microbiology, Health Canada, 1015 Arlington Street, Winnipeg, Manitoba, R3E 3R2) under accession no. IDAC010201-5.

Detail Description Paragraph:

[0066] The parasporal inclusion bodies produced by a sporulated culture of *B. thuringiensis* strain M15 appear roughly spherical when observed under phase-contrast microscopy (FIG. 1A) and are tightly coupled to the spores even in lysed cultures. Further analysis under the transmission electron microscope (TEM), however, reveals that the parasporal inclusion body has a polygonal shape (FIG. 1B). The TEM observation was conducted after the *B. thuringiensis* strain M15 was incubated for 5 days at 30.degree. C. in T3 medium and the samples ultra-thinly sectioned according to Beveridge et al. (1994). Arrows show the roughly spherical

parasporal inclusions tightly bound to the white ovoid spores. In this figure, "S" and "P" denote spore and parasporal inclusion, respectively. Magnification used is of 25,000.times..

Detail Description Paragraph:

[0068] The *B. thuringiensis* strain M15 was grown in T3 medium for 5 days at 30.degree. C. on a rotary shaker to allow crystal protein production. Spores and crystals were separated from each other in the tightly bound parasporal duplexes using an ultrasonic processor model VC130 (Sonics & Materials, Inc., Newtown, Conn., USA) and purified by sucrose density gradient centrifugation as described elsewhere (Thomas and Ellar, 1983). Twenty microliters of the crystal suspension were added to 3 volumes of gel loading buffer (4% SDS, 20% glycerol, 125 mM Tris-HCl, 10% 2-mercaptoethanol, pH 6.8) in a 1.5-ml microtube, incubated at 90.degree. C. for 7 min and centrifuged for 2 min to remove unsolubilized materials. Thirty microliters of the supernatant were loaded on top of 10% SDS-polyacrylamide gels. Discontinuous sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) was performed according to Laemmli and Favre (1973).

Detail Description Paragraph:

[0091] The *B. thuringiensis* Cry-B transformant containing the *B. thuringiensis* M15 parasporal crystal protein gene was incubated in nutrient broth (Bacto Beef Extract 3 g, Bacto Peptone 5 g I-1) at 30.degree. C. for 3 days to allow expression of the toxin gene and crystal formation. The presence of parasporal inclusions was examined by phase-contrast microscopy. When observed under a phase-contrast microscope, the *B. thuringiensis* transformants expressing the cry31Aa2 gene contained, in addition to the spore, a roughly spherical inclusion, whereas no inclusions were found in the *B. thuringiensis* transformant harboring the non-recombinant shuttle vector pHPS9 alone (data not shown). Under the transmission electron microscope (TEM), however, the parasporal inclusion body has a nearly perfect hexagonal shape (FIG. 7). Both inclusions in the transformant, spore and crystal, are separated from each other as opposed to what is found in *B. thuringiensis* strain M15 where they are tightly bound to each other.

Detail Description Paragraph:

[0094] The spore-inclusion mixture was harvested from sporulated cultures and the inclusions were partially purified by a biphasic separation method described in Goodman (1967) using polyethylene glycol 6000 (Wako Pure Chemical, Osaka, Japan) and sodium dextran sulfate 500 (Sigma, St. Louis, Mo.). Inclusions were further purified by sucrose density gradient centrifugation as described in Saitoh et al., (1998a). The purified inclusions were stored at 20.degree. C. until use.

Detail Description Paragraph:

[0120] 10. Goodman, N. S., R. J. Gottfried, and M. H. Rogoff. 1967. Biphasic system for separation of spores and crystals of *Bacillus thuringiensis*. *J. Bacteriol.* 94:485

Detail Description Paragraph:

[0121] 11. Haima, P., Van Sinderen, D., Schotting, H., Bron, S., and Venema, G. (1990). Development of a .beta.-galactosidase .alpha.-complementation system for molecular cloning in *Bacillus subtilis*. *Gene* 86, 63-69.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	EMD	Grant D.
------	-------	----------	-------	--------	----------------	------	-----------	-----------	-------------	--------	-----	----------

2. Document ID: US 20020182690 A1

L3: Entry 2 of 3

File: PGPB

Dec 5, 2002

DOCUMENT-IDENTIFIER: US 20020182690 A1

TITLE: POLYHYDROXYALKANOATE BIOSYNTHESIS ASSOCIATED PROTEINS AND CODING REGION IN BACILLUS MEGATERIUM

Summary of Invention Paragraph:

[0008] A nucleic acid fragment encoding proteins involved in polyhydroxyalkanoate biosynthesis was isolated from *Bacillus megaterium*. Nine nucleic acid sequences and their encoded amino acid sequences are disclosed. Sequences encoding *PhaB* and *PhaC* display not insignificant percent identity and similarity to known acetoacetyl-CoA reductase and polyhydroxyalkanoate synthase proteins, while sequences encoding *PhaP*, *PhaQ*, and *PhaR* do not display significant similarity to known sequences. *YkoY* is similar to known toxic anion resistance proteins; *YkoZ* is similar to known RNA polymerase sigma factors; *YkrM* is similar to known Na^{+} -transporting ATP synthase proteins; and *SspD* matches the known *B. megaterium* spore specific DNA binding protein.

Detail Description Paragraph:

[0142] Primer extension products showed a single band from each reaction, indicating one transcript, while control reactions in which RNA was omitted showed no bands. The extension products run alongside sequencing reaction products obtained with the same primer (FIG. 2C), identified the 5' ends of the transcripts thus allowing the putative promoter sequences at approximately -10 and -35-bp for *phaP*, -Q and -R to be identified. The arrangement of genes in the *pha* cluster of *Bacillus megaterium* is unique among those already published and *phaA* is notably absent. The *phaP*, -Q, -R, -B and -C genes were shown to be in a 4,104-bp region, with *phaP* and -Q transcribed in one orientation, each from a separate promoter, while *phaR*, -B and -C were divergently transcribed from a promoter in front of *phaR*. The putative promoters responsible for transcription of *phaQ* and *phaR*, *phaB* and *phaC* show strong similarity to both *Bacillus subtilis* Sigma A type (34) and *Escherichia coli*, Sigma 70 type promoters (14), which can express constitutively. This is in keeping with previous data for *Alcaligenes eutrophus* showing that *phaC* is constitutively synthesized, but PHA is not constitutively accumulated (19). The third putative promoter in this region, the *phaP* promoter, resembles a Sigma D (SigD) type promoter known to control the expression of a regulon of genes associated with flagellar assembly, chemotaxis and motility (13, 20, 46). In *Bacillus subtilis* Sigma D is expressed in the exponential phase and peaks in late exponential phase of growth. This parallels the pattern of PHA accumulation previously described for *Bacillus megaterium* 11561 (32). However, further experiments are required to test the hypothesis that PHA accumulation is regulated by sigma D or products of its resulting transcripts. The *phaP* gene has 18-bp duplicate sequences that could base-pair to form a rho-independent terminator close to its translational stop codon (FIG. 2B). The fact that the -35 promoter region of *sspD* is within this putative hairpin structure, suggests that transcription of *phaP* and *sspD* could be mutually exclusive, thus allowing the expression of *phaP* to play a regulatory role in the expression of *sspD* (spore specific storage protein).

Detail Description Paragraph:

[0193] 4. Connors, M. J., J. M. Mason, and P. Setlow. 1986. Cloning and nucleotide sequencing of genes for three small, acid soluble proteins *Bacillus subtilis* spores. *J. Bacteriol.*, 166: 417-425.

Detail Description Paragraph:

[0198] 9. Fliss, E. R., A. C. Loshon, and P. Setlow. 1986. Genes for *Bacillus megaterium* small, acid-soluble spore proteins: Cloning and nucleotide sequence of three additional genes from this multigene family. *J. Bacteriol.*, 165: 467-473.

Detail Description Paragraph:

[0199] 10. Fliss, E. R. and P. Setlow. 1984. *Bacillus megaterium* spore protein C-3:

nucleotide sequence of its gene and the amino acid sequence at its spore cleavage site. Gene, 30: 167-172.

Detail Description Paragraph:

[0205] 16. Haima, P., D. van Sinderen, H. Scholting, S. Bron, and G. Venema. 1990. Development of β -galactosidase α -complementation system for molecular cloning in Bacillus subtilis. Gene, 86: 63-69.

Detail Description Table CWU:

5TABLE 4 Sequence homologies Homologies to known and Sequence putative genes (accession no.)^a Identity Similarity Function or putative function ykoY YkoY, B. subtilis (Z99110) 64% 73% Toxic anion resistance protein (24) ykoZ YkoZ, B. subtilis (Z99111) 57% 74% RNA polymerase sigma factor (24) sspD SspD, Bacillus megaterium 100% Spore specific, DNA binding (P10572) protein (4, 10) SspD, B. subtilis (P04833) 73% 87% phaP None PHA inclusion-body structure, shape and size (49) phaQ None Unknown phaR None Unknown phaB FabG, Synechocystis (D90907) 50% 66% Fatty acid biosynthesis (23) PhaB, C. vinosum D (P45375) 48% 64% 3-ketoacyl-CoA reductase (28) FabG, B. subtilis (P51831) 47% 67% Fatty acid biosynthesis (35) phaC PhaC, T. violacea (P45366) 38% 59% PHA synthase (29, 23, 28) PhaC, Synechocystis (D90906) 37% 56% PhaC, C. vinosum (P45370) 35% 55% ykrM YkrM, B. subtilis (Z99111) 55% 71% Na⁺-transporting ATP synthase (24) ^aAccession numbers are SWISS-PROT, EMBL or DDBJ; ^bNone, No discernible similarity to known sequences.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	DDNC	Drawn
------	-------	----------	-------	--------	----------------	------	-----------	-----------	-------------	--------	------	-------

3. Document ID: US 6835820 B2

L3: Entry 3 of 3

File: USPT

Dec 28, 2004

DOCUMENT-IDENTIFIER: US 6835820 B2

TITLE: Polyhydroxyalkanoate biosynthesis associated proteins and coding region in bacillus megaterium

Brief Summary Text (10):

A nucleic acid fragment encoding proteins involved in polyhydroxyalkanoate biosynthesis was isolated from Bacillus megaterium. Nine nucleic acid sequences and their encoded amino acid sequences are disclosed. Sequences encoding PhaB and PhaC display not insignificant percent identity and similarity to known acetoacetyl-CoA reductase and polyhydroxyalkanoate synthase proteins, while sequences encoding PhaP, PhaQ, and PhaR do not display significant similarity to known sequences. YkoY is similar to known toxic anion resistance proteins; YkoZ is similar to known RNA polymerase sigma factors; YkrM is similar to known Na⁺-transporting ATP synthase proteins; and SspD matches the known B. megaterium spore specific DNA binding protein.

Detailed Description Text (139):

Primer extension products showed a single band from each reaction, indicating one transcript, while control reactions in which RNA was omitted showed no bands. The extension products run alongside sequencing reaction products obtained with the same primer (FIG. 2C), identified the 5' ends of the transcripts thus allowing the putative promoter sequences at approximately -10 and -35-bp for phaP, -Q and -R to be identified. The arrangement of genes in the pha cluster of Bacillus megaterium is unique among those already published and phaA is notably absent. The phaP, -Q, -R, -B and -C genes were shown to be in a 4,104-bp region, with phaP and -Q transcribed in one orientation, each from a separate promoter, while phaR, -B and -

C were divergently transcribed from a promoter in front of phaR. The putative promoters responsible for transcription of phaQ and phaR, phaB and phaC show strong similarity to both *Bacillus subtilis* Sigma A type (34) and *Escherichia coli*, Sigma 70 type promoters (14), which can express constitutively. This is in keeping with previous data for *Alcaligenes eutrophus* showing that phaC is constitutively synthesized, but PHA is not constitutively accumulated (19). The third putative promoter in this region, the phaP promoter, resembles a Sigma D (SigD) type promoter known to control the expression of a regulon of genes associated with flagellar assembly, chemotaxis and motility (13, 20, 46). In *Bacillus subtilis* Sigma D is expressed in the exponential phase and peaks in late exponential phase of growth. This parallels the pattern of PHA accumulation previously described for *Bacillus megaterium* 11561 (32). However, further experiments are required to test the hypothesis that PHA accumulation is regulated by sigma D or products of its resulting transcripts. The phaP gene has 18-bp duplicate sequences that could base-pair to form a rho-independent terminator close to its translational stop codon (FIG. 2B). The fact that the -35 promoter region of sspD is within this putative hairpin structure, suggests that transcription of phaP and sspD could be mutually exclusive, thus allowing the expression of phaP to play a regulatory role in the expression of sspD (spore specific storage protein).

Detailed Description Text (204):

The following references, to the extent that they provide exemplary procedural or other details supplementary to those set forth herein, are specifically incorporated herein by reference. 1. Altschul, S. F., T. L. Madden, A. A. Schaffer, J. Zhang, Z. Zhang, W. Miller, and D. J. Lipman. 1997. Gapped BLAST and PSI BLAST: a new generation of protein database search programs. *Nucleic Acids Res.*, 25: 3389-3402. 2. Anderson, A. and E. A. Dawes. 1990. Occurrence, metabolism, metabolic role, and industrial uses of bacterial polyhydroxyalkanoates. *Microbiol Rev.*, 54: 450-472. 3. Cevallos, M. A., S. Encarnacion, A. Leija, Y. Mora, and J. Mora. 1996. Genetic and physiological characterization of a *Rhizobium etli* mutant strain unable to synthesize poly-beta-hydroxybutyrate. *J. Bacteriol.*, 178: 1646-1654. 4. Connors, M. J., J. M. Mason, and P. Setlow. 1986. Cloning and nucleotide sequencing of genes for three small, acid soluble proteins *Bacillus subtilis* spores. *J. Bacteriol.*, 166: 417-425. 5. deSmet, M. J., G. Eggink, B. Witholt, J. Kingma, and H. Wynberg. 1983. Characterization of intracellular inclusions formed by *Pseudomonas oleovorans* during growth on octane. *J. Bacteriol.*, 154: 870-878. 6. Dunlop, W. and A. W. Robards. 1973. Ultrastructural study of poly-.beta.-hydroxybutyrate granules from *Bacillus cereus*. *J. Bacteriol.*, 114: 1271-1280. 7. Eggink, G., P. de Waard, and G. N. M. Huijberts. 1992. The role of fatty acid biosynthesis and degradation in the supply of substrates for poly(3-hydroxyalkanoate) formation in *Pseudomonas putida*. *FEMS Microbiol. Rev.*, 103: 159-164. 8. Ellar, D., D. G. Lundgren, K. Okamura, and R. H. Marchessault. 1968. Morphology of poly-.beta.-hydroxybutyrate granules. *J. Mol. Biol.*, 35: 489-502. 9. Fliss, E. R., A. C. Loshon, and P. Setlow. 1986. Genes for *Bacillus megaterium* small, acid-soluble spore proteins: Cloning and nucleotide sequence of three additional genes from this multigene family. *J. Bacteriol.*, 165: 467-473. 10. Fliss, E. R. and P. Setlow. 1984. *Bacillus megaterium* spore protein C-3: nucleotide sequence of its gene and the amino acid sequence at its spore cleavage site. *Gene*, 30: 167-172. 11. Fuller, R. C., J. P. O'Donnell, J. Saulnier, T. E. Redlinger, J. Foster, and R. W. Lenz. 1992. The supramolecular architecture of the polyhydroxyalkanoate inclusions in *Pseudomonas oleovorans*. *FEMS Microbiol. Rev.*, 103: 279-288. 12. Gemgross, T. U., P. Reilly, J. Stubbe, A. J. Sinskey, and O. P. Peoples. 1993. Immunocytochemical analysis of poly-.beta.-hydroxybutyrate (PHB) synthase enzyme at the surface of PHB granules. *J. Bacteriol.*, 175: 5289-5293. 13. Gilman, M. Z., J. L. Wings, and M. J. Chamberlin. 1981. Nucleotide sequence of two *Bacillus subtilis* promoters used by *Bacillus subtilis* sigma-28 RNA polymerase. *Nucleic Acids Res.*, 9: 5991-6000. 14. Gitt, M. A., L. F. Wang, and R. H. Doi. 1985. A strong sequence homology exists between RNA polymerase sigma factors of *Bacillus subtilis* and *Escherichia coli*. *J. Biol. Chem.*, 260: 7178-7185. 15. Griebel, R., Z. Smith, and M. Merrick. 1968. Metabolism of poly-.beta.-hydroxybutyrate. 1. Purification, composition, and properties of native poly-

.beta.-hydroxybutyrate granules from *Bacillus megaterium*. *Biochem.*, 7: 3676-3681. 16. Haima, P., D. van Sinderen, H. Scholting, S. Bron, and G. Venema. 1990. Development of .beta.-galactosidase .alpha.-complementation system for molecular cloning in *Bacillus subtilis*. *Gene*, 86: 63-69. 17. Haywood, G. W., A. J. Anderson, L. Chu, and E. A. Dawes. 1988. The role of NADH- and NADPH-linked acetoacetyl-CoA reductases in the poly-3-hydroxybutyrate synthesizing organism *Alcaligenes eutrophus*. *FEMS Microbiol. Lett.*, 52: 259-264. 18. Haywood, G. W., A. J. Anderson, L. Chu, and E. A. Dawes. 1988. Characterization of two 3-ketothiolases in the polyhydroxyalkanoate synthesizing organism *Alcaligenes eutrophus*. *FEMS Microbiol. Lett.*, 52: 91-96. 19. Haywood, G. W., A. J. Anderson, and E. A. Dawes. 1989. The importance of PHB-synthase substrate specificity in polyhydroxyalkanoate synthesis by *Alcaligenes eutrophus*. *FEMS Microbiol. Lett.*, 57: 1-6. 20. Helmann, J. D. 1991. Alternative sigma factors and the regulation of flagellar gene expression. *Mol. Microbiol.*, 5: 2875-2882. 21. Huang, A. H. C. 1992. Oil bodies and oleosins in seeds. *Annu. Rev. Plant Physiol. Plant Mol. Biol.*, 43: 177-200. 22. Huisman, G. W., E. Wonink, R. Meima, B. Kazemier, P. Terpstra, and B. Witholt. 1991. Metabolism of poly(3-hydroxyalkanoates) (PHAs) by *Pseudomonas oleovorans*. *J. Biol. Chem.*, 266: 2191-2198. 23. Kaneko, T. et al. 1996. Sequence analysis of the genome of the unicellular cyanobacterium *Synechocystis* sp. strain PCC6803. II. Sequence determination of the entire genome and assignment of potential protein-coding regions. *DNA Res.*, 3: 109-136. 24. Kunst, N. et al. 1997. The complete genome sequence of the Gram-positive bacterium *Bacillus subtilis*. *Nature*, 390: 249-256. 25. Lauzier, C., R. H. Marchessault, P. Smith, and H. Chanzy. 1992. Structural study of isolated poly(.beta.-hydroxybutyrate) granules. *Polymer*, 33: 823-827. 26. Lee, S. Y. 1995. Bacterial polyhydroxyalkanoates. *Biotechnology & Engineering*, 49: 1-14. 27. Liebergesell, M., B. Schmidt, and A. Steinbuchel. 1992. Isolation and identification of granule-associated proteins relevant for poly(hydroxyalkanoic acid) biosynthesis in *Chromatium vinosum* D. *FEMS Microbiol. Lett.*, 99: 227-232. 28. Liebergesell, M. and A. Steinbuchel. 1992. Cloning and nucleotide sequences of genes relevant for biosynthesis of poly(3-hydroxybutyric acid) in *Chromatium vinosum* strain D. *Eur. J. Biochem.*, 209: 135-150. 29. Liebergesell, M. and A. Steinbuchel. 1993. Cloning and molecular analysis of the poly (3-hydroxybutyric acid) biosynthetic genes of *Thiocystis violacea*. *Appl. Microbiol. Biotechnol.*, 38: 493-501. 30. Lundgren, D. G., R. M. Pfister, and J. M. Merrick. 1964. Structure of poly-.beta.-hydroxybutyric acid granules. *J. Gen. Microbiol.*, 34: 441-446. 31. Magni, C., P. Marini, and D. de Mendoza. 1995. Extraction of RNA from gram-positive bacteria. *Biotechniques*, 19: 882-884. 32. McCool, G. J., T. Fernandez, N. Li, and M. C. Cannon. 1996. Polyhydroxyalkanoate inclusion-body growth and proliferation in *Bacillus megaterium*. *FEMS Microbiol. Lett.*, 137: 41-48. 33. Miller, J. H. 1972. Experiments in molecular genetics. Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y.: 34. Moran, C. P. Jr., N. Lang, S. F. J. LeGrice, G. Lee, M. Stephens, A. L. Sonnenschein, J. Pero, and R. Losick. 1982. Nucleotide sequences that signal the initiation of transcription and translation in *Bacillus subtilis*. *Mol. Gen. Genet.*, 186: 339-346. 35. Morbidoni, H. R., D. de Mendoza, and J. E. Cronan. 1996. *Bacillus subtilis* acyl carrier protein is encoded in a cluster of lipid biosynthesis genes. *J. Bacteriol.*, 178: 4794-4800. 36. Pieper-Furst, U., M. H. Madkour, F. Mayer, and A. Steinbuchel. 1994. Purification and characterization of a 14-kilodalton protein that is bound to the surface of polyhydroxyalkanoic acid granules in *Rhodococcus ruber*. *J. Bacteriol.*, 176: 4328-4337. 37. Pieper-Furst, U., M. H. Madkour, F. Mayer, and A. Steinbuchel. 1995. Identification of the region of a 14-kilodalton protein of *Rhodococcus ruber* that is responsible for the binding of this Phasin to polyhydroxyalkanoic acid granules. *J. Bacteriol.*, 177: 2513-2523. 38. Sambrook, J., E. F. Fritsch & T. Maniatis. 1989. Molecular Cloning: A Laboratory Manual., 2nd ed. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. 39. Shark, K. B., F. D. Smith, P. R. Harpending, and J. L. Rasmussen. 1991. Biolistic transformation of a prokaryote, *Bacillus megaterium*. *Appl. Environ. Microbiol.*, 57: 480-485. 40. Simon, R., Priefer, U. & Puhler, A. 1983. In A. Puhler (Ed.), Molecular genetics of the bacteria-plant interaction. Springer, Berlin. p. 98-106. 41. Steinbuchel, A. 1991. Polyhydroxyalkanoic acids. p. 123-213. In D. Byrom (Ed.), Biomaterials, novel materials from biological sources. Macmillan

Publishers Ltd., Basingstoke, England. 42. Steinbuchel, A., K. Aerts, W. Babel, C. Follner, M. Liebergesell, M. H. Madkour, F. Mayer, U. Pieper-Furst, A. Pries, H. E. Valentin, and R. Wieczorek. 1995. Considerations on the structure and biochemistry of bacterial polyhydroxyalkanoic acid inclusions. *Can. J. Microbiol.*, 41: 94-105. 43. Steinbuchel, A., E. Hustedt, M. Liebergesell, U. Pieper, A. Timm, and H. Valentin. 1992. Molecular basis for biosynthesis and accumulation of polyhydroxyalkanoic acids in bacteria. *FEMS Microbiol. Rev.*, 103: 217-230. 44. Steinbuchel, A. and H. G. Schlegel. 1991. Physiology and molecular genetics of poly (beta-hydroxyalkanoic acid) synthesis in *Alcaligenes eutrophus*. *Mol. Microbiol.*, 5: 535-542. 45. Steinbuchel, A. and H. E. Valentin. 1995. Diversity of bacterial polyhydroxyalkanoic acids. *FEMS Microbiol. Lett.*, 128: 219-228. 46. Vary, P. 1993. The genetic map of *Bacillus megaterium*, p. 475-481. In A. L. Sonenshein, J. A. Hoch & R. Losick (Eds.), *Bacillus subtilis and other gram positive bacteria*. American Society for Microbiology, Washington, D.C. 47. Wang, W. S. and D. G. Lundgren. 1969. Poly-beta-hydroxybutyrate in the chemolithotrophic bacterium *Ferrobacillus ferrooxidans*. *J. Bacteriol.*, 97: 947-950.

Detailed Description Paragraph Table (5):

TABLE 4 Sequence homologies Homologies to known and Sequence putative genes (accession no.).sup.a Identity Similarity Function or putative function ykOY YkOY, *B. subtilis* (Z99110) 64% 73% Toxic anion resistance protein (24) ykOZ YkOZ, *B. subtilis* (Z99111) 57% 74% RNA polymerase sigma factor (24) sspD SspD, *Bacillus megaterium* 100% Spore specific, DNA binding (P10572) protein (4, 10) SspD, *B. subtilis* (P04833) 73% 87% phaP None PHA inclusion-body structure, shape and size (49) phaQ None Unknown phaR None Unknown phaB FabG, *Synechocystis* (D90907) 50% 66% Fatty acid biosynthesis (23) PhaB, *C. vinosum* D (P45375) 48% 64% 3-ketoacyl-CoA reductase (28) FabG, *B. subtilis* (P51831) 47% 67% Fatty acid biosynthesis (35) phaC PhaC, *T. violacea* (P45366) 38% 59% PHA synthase (29, 23, 28) PhaC, *Synechocystis* (D90906) 37% 56% PhaC, *C. vinosum* (P45370) 35% 55% ykrM YkrM, *B. subtilis* (Z99111) 55% 71% Na.sup.+ -transporting ATP synthase (24) .sup.a Accession numbers are SWISS-PROT, EMBL or DDBJ; .sup.b None, No discernible similarity to known sequences.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Document	Document	Document	Claims	DDNC	Drawn
------	-------	----------	-------	--------	----------------	------	-----------	----------	----------	----------	--------	------	-------

Clear	Generate Collection	Print	Fwd Refs	Bkwd Refs	Generate OACS
-------	---------------------	-------	----------	-----------	---------------

Term	Documents
SPORE	18401
SPORES	29862
(2 AND SPORE) . PGPB, USPT, USOC, EPAB, JPAB, DWPI.	3
(L2 AND SPORE) . PGPB, USPT, USOC, EPAB, JPAB, DWPI.	3

Display Format: [-]

[Previous Page](#) [Next Page](#) [Go to Doc#](#)

eutrophus. *FEMS Microbiol. Lett.*, 52: 259-264. 18. Haywood, G. W., A. J. Anderson, L. Chu, and E. A. Dawes. 1988. Characterization of two 3-ketothiolases in the polyhydroxyalkanoate synthesizing organism *Alcaligenes eutrophus*. *FEMS Microbiol. Lett.*, 52: 91-96. 19. Haywood, G. W., A. J. Anderson, and E. A. Dawes. 1989. The importance of PHB-synthase substrate specificity in polyhydroxyalkanoate synthesis by *Alcaligenes eutrophus*. *FEMS Microbiol. Lett.*, 57: 1-6. 20. Helmann, J. D. 1991. Alternative sigma factors and the regulation of flagellar gene expression. *Mol. Microbiol.*, 5: 2875-2882. 21. Huang, A. H. C. 1992. Oil bodies and oleosins in seeds. *Annu. Rev. Plant Physiol. Plant Mol. Biol.*, 43: 177-200. 22. Huisman, G. W., E. Wonink, R. Meima, B. Kazemier, P. Terpstra, and B. Witholt. 1991. Metabolism of poly(3-hydroxyalkanoates) (PHAs) by *Pseudomonas oleovorans*. *J. Biol. Chem.*, 266: 2191-2198. 23. Kaneko, T. et al. 1996. Sequence analysis of the genome of the unicellular cyanobacterium *Synechocystis* sp. strain PCC6803. II. Sequence determination of the entire genome and assignment of potential protein-coding regions. *DNA Res.*, 3: 109-136. 24. Kunst, N. et al. 1997. The complete genome sequence of the Gram-positive bacterium *Bacillus subtilis*. *Nature*, 390: 249-256. 25. Lauzier, C., R. H. Marchessault, P. Smith, and H. Chanzy. 1992. Structural study of isolated poly(.beta.-hydroxybutyrate) granules. *Polymer*, 33: 823-827. 26. Lee, S. Y. 1995. Bacterial polyhydroxyalkanoates. *Biotechnology & Engineering*, 49: 1-14. 27. Liebergesell, M., B. Schmidt, and A. Steinbuchel. 1992. Isolation and identification of granule-associated proteins relevant for poly(hydroxyalkanoic acid) biosynthesis in *Chromatium vinosum* D. *FEMS Microbiol. Lett.*, 99: 227-232. 28. Liebergesell, M. and A. Steinbuchel. 1992. Cloning and nucleotide sequences of genes relevant for biosynthesis of poly(3-hydroxybutyric acid) in *Chromatium vinosum* strain D. *Eur. J. Biochem.*, 209: 135-150. 29. Liebergesell, M. and A. Steinbuchel. 1993. Cloning and molecular analysis of the poly (3-hydroxybutyric acid) biosynthetic genes of *Thiocystis violacea*. *Appl. Microbiol. Biotechnol.*, 38: 493-501. 30. Lundgren, D. G., R. M. Pfister, and J. M. Merrick. 1964. Structure of poly-.beta.-hydroxybutyric acid granules. *J. Gen. Microbiol.*, 34: 441-446. 31. Magni, C., P. Marini, and D. de Mendoza. 1995. Extraction of RNA from gram-positive bacteria. *Biotechniques*, 19: 882-884. 32. McCool, G. J., T. Fernandez, N. Li, and M. C. Cannon. 1996. Polyhydroxyalkanoate inclusion-body growth and proliferation in *Bacillus megaterium*. *FEMS Microbiol. Lett.*, 137: 41-48. 33. Miller, J. H. 1972. Experiments in molecular genetics. *Cold Spring Harbor Laboratory*, Cold Spring Harbor, N.Y.: 34. Moran, C. P. Jr., N. Lang, S. F. J. LeGrice, G. Lee, M. Stephens, A. L. Sonnenschein, J. Pero, and R. Losick. 1982. Nucleotide sequences that signal the initiation of transcription and translation in *Bacillus subtilis*. *Mol. Gen. Genet.*, 186: 339-346. 35. Morbidoni, H. R., D. de Mendoza, and J. E. Cronan. 1996. *Bacillus subtilis* acyl carrier protein is encoded in a cluster of lipid biosynthesis genes. *J. Bacteriol.*, 178: 4794-4800. 36. Pieper-Furst, U., M. H. Madkour, F. Mayer, and A. Steinbuchel. 1994. Purification and characterization of a 14-kilodalton protein that is bound to the surface of polyhydroxyalkanoic acid granules in *Rhodococcus ruber*. *J. Bacteriol.*, 176: 4328-4337. 37. Pieper-Furst, U., M. H. Madkour, F. Mayer, and A. Steinbuchel. 1995. Identification of the region of a 14-kilodalton protein of *Rhodococcus ruber* that is responsible for the binding of this Phasin to polyhydroxyalkanoic acid granules. *J. Bacteriol.*, 177: 2513-2523. 38. Sambrook, J., E. F. Fritsch & T. Maniatis. 1989. *Molecular Cloning: A Laboratory Manual*, 2nd ed. *Cold Spring Harbor Laboratory Press*, Cold Spring Harbor, N.Y. 39. Shark, K. B., F. D. Smith, P. R. Harpending, and J. L. Rasmussen. 1991. Biolistic transformation of a prokaryote, *Bacillus megaterium*. *Appl. Environ. Microbiol.*, 57: 480-485. 40. Simon, R., Priefer, U. & Puhler, A. 1983. In A. Puhler (Ed.), *Molecular genetics of the bacteria-plant interaction*. Springer, Berlin. p. 98-106. 41. Steinbuchel, A. 1991. Polyhydroxyalkanoic acids. p. 123-213. In D. Byrom (Ed.), *Biomaterials, novel materials from biological sources*. Macmillan Publishers Ltd., Basingstoke, England. 42. Steinbuchel, A., K. Aerts, W. Babel, C. Follner, M. Liebergesell, M. H. Madkour, F. Mayer, U. Pieper-Furst, A. Pries, H. E. Valentin, and R. Wieczorek. 1995. Considerations on the structure and biochemistry of bacterial polyhydroxyalkanoic acid inclusions. *Can. J. Microbiol.*, 41: 94-105. 43. Steinbuchel, A., E. Hustede, M. Liebergesell, U. Pieper, A. Timm, and H. Valentin. 1992. Molecular basis for biosynthesis and accumulation of

polyhydroxyalkanoic acids in bacteria. FEMS Microbiol. Rev., 103: 217-230. 44. Steinbuchel, A. and H. G. Schlegel. 1991. Physiology and molecular genetics of poly (. β .-hydroxyalkanoic acid) synthesis in *Alcaligenes eutrophus*. Mol. Microbiol., 5: 535-542. 45. Steinbuchel, A. and H. E. Valentin. 1995. Diversity of bacterial polyhydroxyalkanoic acids. FEMS Microbiol. Lett., 128: 219-228. 46. Vary, P. 1993. The genetic map of *Bacillus megaterium*, p. 475-481. In A. L. Sonenshein, J. A. Hoch & R. Losich (Eds.), *Bacillus subtilis and other gram positive bacteria*. American Society for Microbiology, Washington, D.C. 47. Wang, W. S. and D. G. Lundgren. 1969. Poly-. β .-hydroxybutyrate in the chemolithotrophic bacterium *Ferrobacillus ferrooxidans*. J. Bacteriol., 97: 947-950.

[Previous Doc](#)[Next Doc](#)[Go to Doc#](#)

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2006/000582

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K39/39 C12N15/87

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K C12R C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>SIRARD J C ET AL: "Intracytoplasmic delivery of listeriolysin O by a vaccinal strain of <i>Bacillus anthracis</i> induces CD8-mediated protection against <i>Listeria monocytogenes</i>." JOURNAL OF IMMUNOLOGY, vol. 159, no. 9, 1 November 1997 (1997-11-01), pages 4435-4443, XP002943106 ISSN: 0022-1767 the whole document abstract page 4442, right-hand column, lines 21-28</p>	1-21
Y	<p>WO 03/074682 A (ROYAL HOLLOWAY UNIVERSITY OF LONDON; CUTTING, SIMON, MICHAEL) 12 September 2003 (2003-09-12) the whole document</p>	1-21 -/-

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the International search	Date of mailing of the International search report
1 June 2006	22/06/2006
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel: (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer van de Kamp, M

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2006/000582

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DIETRICH G ET AL: "From evil to good: a cytolysin in vaccine development." TRENDS IN MICROBIOLOGY. JAN 2001, vol. 9, no. 1, January 2001 (2001-01), pages 23-28, XP002382792 ISSN: 0966-842X the whole document page 25, right-hand column, lines 18-47 -----	1-21
Y	WO 03/074681 A (ROYAL HOLLOWAY UNIVERSITY OF LONDON; CUTTING, SIMON, MICHAEL) 12 September 2003 (2003-09-12) the whole document -----	1-21
Y	DUC L H ET AL: "Bacterial spores as vaccine vehicles" INFECTION AND IMMUNITY, vol. 71, no. 5, May 2003 (2003-05), pages 2810-2818, XP009011619 ISSN: 0019-9567 the whole document -----	1-21
Y	DUC L H ET AL: "Germination of the spore in the gastrointestinal tract provides a novel route for heterologous antigen delivery" VACCINE, vol. 21, no. 27-30, 1 October 2003 (2003-10-01), pages 4215-4224, XP004462821 ISSN: 0264-410X the whole document -----	1-21
Y	MAURIELLO E M F ET AL: "Display of heterologous antigens on the <i>Bacillus subtilis</i> spore coat using CotC as a fusion partner" VACCINE, vol. 22, no. 9-10, 12 March 2004 (2004-03-12), pages 1177-1187, XP004493381 ISSN: 0264-410X the whole document -----	1-21
Y	DUC L H ET AL: "Intracellular fate and immunogenicity of <i>B. subtilis</i> spores" VACCINE, vol. 22, no. 15-16, 7 May 2004 (2004-05-07), pages 1873-1885, XP004505510 ISSN: 0264-410X the whole document ----- -/-	1-21

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2006/000582

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	CUTTING S. M.: "Spores as oral vaccines" 2004, IN: BACTERIAL SPORE FORMERS. EDITOR(S): RICCA, EZIO; HENRIQUES, ADRIANO O.; CUTTING, SIMON M. PUBLISHER: HORIZON BIOSCIENCE, WYMONDHAM, UK. CODEN: 69GBOG; ISBN: 1-904933-02-5 , XP008064832 page 201 - page 206	1-21
Y	BARÁK I ET AL: "From fundamental studies of sporulation to applied spore research." MOLECULAR MICROBIOLOGY. JAN 2005, vol. 55, no. 2, January 2005 (2005-01), pages 330-338, XP002382791 ISSN: 0950-382X the whole document abstract page 336, left-hand column, line 52 - right-hand column, line 14	1-21
Y	BIELECKI J ET AL: "Bacillus subtilis expressing a haemolysin gene from Listeria monocytogenes can grow in mammalian cells." NATURE, vol. 345, no. 6271, 10 May 1990 (1990-05-10), pages 175-176, XP001183398 ISSN: 0028-0836 the whole document	1-21
Y	WO 00/09733 A (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA) 24 February 2000 (2000-02-24) the whole document page 5, line 28 - page 6, line 1	1-21
Y	HIGGINS D E ET AL: "Bacterial delivery of DNA evolves" NATURE BIOTECHNOLOGY, NATURE PUBLISHING GROUP, NEW YORK, NY, US, vol. 16, February 1998 (1998-02), pages 138-139, XP000700246 ISSN: 1087-0156 the whole document page 139, right-hand column, lines 19-49	1-21
Y	US 5 830 702 A (PORTNOY ET AL) 3 November 1998 (1998-11-03) the whole document	1-21

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/GB2006/000582

Patent document cited in search report	Publication date		Patent family member(s)	Publication date
WO 03074682	A 12-09-2003	AU CN EP JP US	2003217007 A1 1639321 A 1490473 A1 2005522195 T 2005232947 A1	16-09-2003 13-07-2005 29-12-2004 28-07-2005 20-10-2005
WO 03074681	A 12-09-2003	AU CN EP JP US	2003214391 A1 1639322 A 1495110 A1 2005519123 T 2005287168 A1	16-09-2003 13-07-2005 12-01-2005 30-06-2005 29-12-2005
WO 0009733	A 24-02-2000	AU EP US US	5674099 A 1105512 A1 6004815 A 6287556 B1	06-03-2000 13-06-2001 21-12-1999 11-09-2001
US 5830702	A 03-11-1998		NONE	

AU2003215062A1		WO2003066818	Based on
EP 1487853A2	February 6, 2003	2003EP-0710878	
EP 1487853A2	February 6, 2003	2003WO-US03534	
EP 1487853A2		WO2003066818	Based on
JP2005516613W	February 6, 2003	2003JP-0566169	
JP2005516613W	February 6, 2003	2003WO-US03534	
JP2005516613W		WO2003066818	Based on
US20050209448A1	February 8, 2002	2002US-355258P	Provisional
US20050209448A1	February 6, 2003	2003WO-US03534	
US20050209448A1	April 7, 2005	2005US-0502667	
CN 1639183A	February 6, 2003	2003CN-0804758	